IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

A. NATTERMANN & Cie GmbH, AVENTIS BEHRING L.L.C., and AVENTIS PHARMA S.A.,	)	
Plaintiffs and Counterclaim Defendants,	)	Civil Action No.: 03-2268 ABB
v.	)	
BAYER CORPORATION and BAYER HEALTHCARE LLC,	)	
Defendants and Counterclaimants,	)	
v.	)	
AVENTIS BEHRING GmbH, ZLB BEHRING L.L.C., and ZLB BEHRING GmbH	)	
Counterclaim Defendants.	)	

FILED
AUG 24 2006
MICHAEL E. KUNZ, Clerk
By Dep. Clerk

FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs and Counterclaim Defendants A. Nattermann & Cie GmbH, Aventis Behring L.L.C., and Aventis Pharma S.A. and Counterclaim Defendants Aventis Behring GmbH, ZLB Behring L.L.C., and ZLB Behring GmbH (collectively "Plaintiffs"), for their First Amended Complaint against Defendants, Bayer Corporation and Bayer Healthcare LLC ("Defendants" or "Bayer"), hereby state as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement of United States Patent No. 5,565,427 ("the '427 patent"), arising under the patent laws of the United States, 35 U.S.C. § 100 et seq. This action relates to Defendants' commercial manufacture, offer for sale, and sale by

Defendants of their KOGENATE® FS product, which contains a stabilized solution with Factor VIII:C activity.

THE PARTIES

2. Plaintiff and Counterclaim Defendant A. Nattermann & Cie GmbH is a corporation organized under the laws of Germany, with its principal place of business at Nattermannallee 1, D-50829 Cologne, Germany.

3. Plaintiff and Counterclaim Defendant Aventis Behring L.L.C. (currently ZLB Behring L.L.C.) was formerly a corporation organized under the laws of Delaware, with its principal place of business at 1020 First Avenue, King of Prussia, Pennsylvania 19406.

4. Plaintiff and Counterclaim Defendant Aventis Pharma S.A. is a corporation organized under the laws of France, with its corporate headquarters at 20, avenue Raymond Aron, 92160 Antony, France.

5. Counterclaim Defendant Aventis Behring GmbH (currently ZLB Behring GmbH) was formerly a corporation organized and existing under the laws of Germany, with its principal place of business at Emil-von-Behring-Strasse 76, 35401 Marburg, Germany.

6. Counterclaim Defendant ZLB Behring L.L.C. (formerly Aventis Behring L.L.C.) is a corporation organized under the laws of Delaware, with its principal place of business at 1020 First Avenue, King of Prussia, Pennsylvania 19406.

7. Counterclaim Defendant ZLB Behring GmbH (formerly Aventis Behring GmbH) is a corporation organized and existing under the laws of Germany, with its principal place of business at Emil-von-Behring-Strasse 76, 35401 Marburg, Germany.

8. Upon information and belief, Defendant Bayer Corporation is an Indiana Corporation having its corporate offices and principal place of business at 100 Bayer Rd., Building 4, Pittsburgh, Pennsylvania 15205.

9. Upon information and belief, Defendant Bayer Healthcare LLC is a Delaware Corporation having its corporate offices and principal place of business at 79 T.W. Alexander Dr., 4101 Research Commons, P.O. Box 13887, Research Triangle, North Carolina 27709.

JURISDICTION AND VENUE

10. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a).

11. This Court has jurisdiction over the Defendants because, on information and belief, one or both of the Defendants purposefully have conducted and continue to conduct business in this judicial district, have placed the accused product in the stream of commerce knowing and intending this judicial district was and is a likely destination of this product, have caused injury to Plaintiffs in this judicial district, have committed acts of infringement in this judicial district, and have corporate offices in Pennsylvania.

12. Upon information and belief, this Court has personal jurisdiction over Defendants.

13. Upon information and belief, venue is proper in this judicial district under 28 U.S.C. §§ 1391(c) and 1400(b).

FIRST COUNT FOR PATENT INFRINGEMENT

14. The '427 patent, entitled "Stabilized Factor VIII Preparations," was duly and legally issued to Behringwerke Aktiengesellschaft, as assignee of inventor Wilfried Freudenberg, by the United States Patent and Trademark Office ("PTO") on October 15, 1996. A true and correct copy of the '427 patent is attached as Exhibit A. Behringwerke Aktiengesellschaft merged with Hoechst Aktiengesellschaft, and Hoechst Aktiengesellschaft subsequently assigned

the '427 patent to Centeon Pharma GmbH, which became Aventis Behring GmbH upon the merger of Hoechst and Rhone Poulenc to form Aventis.

15. Aventis Behring GmbH assigned the rights to the '427 patent to A. Nattermann & Cie GmbH.

16. Aventis Pharma S.A. is the present owner of the '427 patent as a result of an assignment from A. Nattermann & Cie GmbH.

17. On July 23, 2002, the PTO issued a first Reexamination Certificate to assignee Aventis Behring GmbH, confirming without amendment the patentability of the claims of the '427 patent. A true and correct copy of the Reexamination Certificate is attached as Exhibit B.

18. On October 21, 2003, a Second Request for Reexamination was filed in the PTO, together with an Amendment Pursuant to 37 C.F.R. §§ 1.510(e) and 1.530(d), adding new claims 14-22. This reexamination is currently pending before the PTO. A Notice of Intent to Issue *Ex Parte* Reexamination Certificate ("NIRC") issued October 11, 2005. A true and correct copy of the NIRC is attached as Exhibit C.

19. The '427 patent discloses and claims, *inter alia,* stabilized solutions with factor VIII:C activity and methods of manufacturing such stabilized solutions.

20. On information and belief, Bayer has knowledge of the '427 patent.

21. On April 7, 1998, Bayer Corporation entered into a Supply Agreement with Aventis Behring L.L.C. (previously known as Centeon L.L.C. and now known as ZLB Behring L.L.C.), whereby Bayer Corporation agreed to supply Aventis Behring L.L.C. with an improved antihemophilic Factor VIII (Recombinant) protein to be formulated as a sterile, stable, purified, freeze-dried concentrate, purified and formulated without the use of albumin.

22. Based on information available from the United States Food and Drug Administration's ("FDA") website (www.fda.gov), on June 26, 2000, Bayer Corporation obtained FDA approval to manufacture, use, offer to sell and sell in the United States an improved antihemophilic Factor VIII (Recombinant) protein formulated as a sterile, stable, purified, freeze-dried concentrate, purified and formulated without the use of albumin, under the trademark KOGENATE® FS.

23. Through March 31, 2004, Bayer supplied its KOGENATE® FS product to Aventis Behring L.L.C., who then sold the product under the trademark HELIXATE® FS.

24. From April 1, 2004 to about September 2004, Bayer supplied its KOGENATE® FS product to successor ZLB Behring L.L.C., who then sold the product under the trademark HELIXATE® FS.

25. On information and belief, Bayer manufactured its KOGENATE® FS product in California.

26. Bayer did not take a license under the '427 patent to manufacture, offer for sale, and sell its KOGENATE® FS product to parties other than Aventis Behring L.L.C. or ZLB Behring L.L.C.

27. Bayer's use, manufacture, offering for sale, and sale of its KOGENATE® FS product to parties other than Aventis Behring L.L.C. or ZLB Behring L.L.C. constitutes infringement of the '427 patent under 35 U.S.C. § 271.

DAMAGES AND OTHER HARM SUFFERED BY PLAINTIFFS

28. Bayer's acts of infringement have damaged Plaintiffs in an amount not yet determined.

29. Upon information and belief, Bayer's acts of infringement constitute willful infringement, entitling Plaintiffs to treble damages and attorneys' fees.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter judgment in its favor, and against Bayer, on the patent infringement claim set forth above, and award relief as follows:

(1) find Bayer liable for infringing the '427 patent by its making, using, selling, and offering for sale to third parties its KOGENATE® FS product;

(2) find that Bayer's infringement has been willful;

(3) award Plaintiffs damages adequate to compensate them for the aforesaid infringement, together with prejudgment interest thereon;

(4) treble such damages under 35 U.S.C. § 284 because of the willful infringement of Bayer;

(5) award Plaintiffs their reasonable attorney fees and the costs of this action under 35 U.S.C. § 285; and

(6) award Plaintiffs such further and additional relief as this Court may deem just and proper.

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Attorneys for Plaintiffs

Dated: August 24, 2006

CERTIFICATE OF SERVICE

I, Charles S. Marion, hereby certify that on this 24th day of August 2006, a true and correct copy of the foregoing First Amended Complaint was served via facsimile and Federal Express, upon the following:

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EXHIBIT A

US005565427A

United States Patent [19]

Freudenberg

[11] **Patent Number: 5,565,427**

[45] **Date of Patent: Oct. 15, 1996**

[54] **STABILIZED FACTOR VIII PREPARATIONS**

[75] Inventor: **Wilfried Freudenberg**, Cölbe-Schönstadt, Germany

[73] Assignee: **Behringwerke Aktiengesellschaft**, Marburg, Germany

[21] Appl. No.: **235,241**

[22] Filed: **Apr. 29, 1994**

Related U.S. Application Data

[63] Continuation of Ser. No. 82,911, Jun. 29, 1993, abandoned, which is a continuation of Ser. No. 864,610, Apr. 7, 1992, abandoned.

[30] **Foreign Application Priority Data**

Apr. 9, 1991 [DE] Germany 41 11 393.4

[51] **Int. Cl.**[6] **A61K 35/14**; C07K 1/00; C07K 14/00

[52] **U.S. Cl.** **514/12**; 514/21; 530/383

[58] **Field of Search** 530/383; 514/12, 514/21

[56] **References Cited**

U.S. PATENT DOCUMENTS

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Meyers, R. et al., "Large Scale Preparation of a Highly Purified Solvent–Detergent Treated Factor VIII Concentrate," VOX Sang. vol. 60, pp. 141–147 (1991).

Primary Examiner—Elizabeth C. Weimar
Assistant Examiner—P. Lynn Touzeau
Attorney, Agent, or Firm—Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

[57] **ABSTRACT**

The invention relates to stabilized solutions with F VIII coagulation activity, to a process for the preparation thereof and to the use thereof.

13 Claims, No Drawings

STABILIZED FACTOR VIII PREPARATIONS

This application is a continuation of application Ser. No. 08/082,911 filed Jun. 29, 1993, now abandoned, which is a continuation of application Ser. No. 07/864,610, filed Apr. 7, 1992, abandoned.

The invention relates to stabilized solutions with F VIII coagulation activity, to a process for the preparation thereof and to the use thereof.

Coagulation factor VIII:C (F VIII:C) is a plasma protein and essential for the process of the intrinsic pathway of blood coagulation. A deficiency or a defect in blood coagulation factor VIII:C results in a life-threatening disturbance of blood coagulation, hemophilia A. Concentrates of F VIII:C from human plasma or genetically engineered F VIII:C are employed for the therapy of hemophilia A.

These F VIII products differ in respect of their purity, i.e. the presence of proteins which do not have coagulation activity in addition to the active substance F VIII:C. A F VIII which has more than 1000 U/mg before stabilization with albumin is called very high purity F VIII (VHP F VIII:C) (WHO, Expert Committee on Biological Standardization).

Such VHP F VIII:C have potential advantages in the treatment of hemophilia. These are the freedom from viruses and a very small content of foreign protein, which means less stress on the immune system of the patients after administration of these concentrates. The advantage which is possible per se, of less stress on the immune system of a hemophiliac patient by administration of a F VIII preparation with high specific activity, is, however, cancelled out by addition of high albumin concentrations to the highly purified product in order to stabilize the VHP F VIII. This addition of albumin means that the highly purified F VIII concentrates reach specific activities of only 3–10 U/mg in the final formulation thereof.

Although addition of albumin entails only a slight risk with respect to virus safety, it has to be borne in mind, however, that with albumin whose purity averages 95% once again unwanted concomitant proteins are administered to the patient and may stress his immune system.

High purity F VIII product: which dispense with addition of albumin for stabilization of F VIII are known (Schwinn, Smith & Wolter, Drug. Res. 39 (1989), 1302). These products reach specific activities of about 100 U/mg of protein. Based on a maximum achievable F VIII activity of about 5000 U/mg, this means that only about 2% of the protein content of these preparations comprises F VIII:C protein. It is to be assumed in this case that this 2% F VIII:C is stabilized by the 98% concomitant proteins, because a large part of these concomitant proteins is likely to comprise yon Willebrand Factor (vWF). It is known that von Willebrand Factor has a stabilizing action on F VIII:C.

The situation is different with very high purity products which have specific activities which, before albumin stabilization, are usually more than 25 times higher than for high purity products, and the vWF content thereof is very low. This low vWF content is no longer able to ensure adequate F VIII stabilization so that the F VIII activity in solutions which are not stabilized with albumin rapidly decreases.

The object of the present invention was therefore to provide a process which makes it possible to prepare a highly concentrated, physiologically tolerated solution of a VHP F VIII:C product, which solution requires no addition of proteins for stabilization.

This object is achieved according to the invention by adding an amino acid or one of its salts, derivatives or homologs to a VHP F VIII:C preparation. It is possible to add L- and/or D-amino acids. Particular suitable are arginine, lysine, ornithine, guanidinoacetic acid or others whose common feature is a basic group in the form of an amino and/or guanidino group.

The invention therefore relates to a solution with factor VIII:C activity containing an amino acid or one of its salts or derivatives and, ;here appropriate, a detergent or an organic polymer.

Preferred embodiments are:

a solution wherein the amino acid is a natural amino acid;

a solution wherein the amino acid is a basic amino acid;

a solution which contains arginine and glycine;

a solution wherein the concentration of the amino acid is 0.001 to 1 mol/l;

a solution which additionally contains an organic polymer or a nonionic detergent;

a solution wherein the F VIII:C activity derives from human factor VIII in its form which occurs in plasma or from a genetically engineered factor VIII:C or a derivative of these;

and a solution wherein the specific F VIII:C activity is at least 1000 IU/mg.

Improved stabilization is achieved by combination of amino acids or their derivatives or with a nonionic detergent such as ®Polysorbate 20 or ®Polysorbate 80 or an organic polymer such as polyethylene glycol 1500.

A combination of the amino acids arginine and glycine, preferably 0.01 to 1 mol/l, with the nonionic detergent ®Tween 80, preferably 0.001 to 0.5% (v/v), and with a neutral sugar such as sucrose, preferably 0.1 to 10%, has proven particularly suitable for the preparation of a stable, albumin-free VHP F VIII:C solution.

The pH of a solution of this type is adjusted to between pH 5.5 and 8.5, preferably between pH 6.5 and 7.5, by means of an organic acid, preferably 10% strength acetic acid.

The invention also relates to a pharmaceutical containing a solution of this type. Besides a solution of this type, this pharmaceutical can contain customary, pharmaceutically compatible, stabilizing and/or buffering substances, especially a carbohydrate.

The invention likewise relates to a process for the preparation of a solution of this type, wherein an amino acid or one of its salts or derivatives and, where appropriate, an organic polymer or a detergent is added to a solution with factor VIII:C activity.

The advantageous effect of the process according to the invention can be shown, for example, for a F VIII:C preparation which has been purified by chromatography on monoclonal anti-F VIII:C antibodies, it being possible for the F VIII:C to be both obtained from plasma and genetically engineered, for example in CHO (Chinese Hamster Ovary) cells. This entails, for example, equal parts of a solution of the abovementioned substances being added to the eluate from the monoclonal antibody column, and subsequently the latter being dialyzed against this solution. The stabilized F VIII:C preparation obtained in this way can be sterilized by filtration and bottled with low method-related losses. A lyophilizate of this preparation obtained in this way has unchanged high F VIII:C activities after dissolution.

It is possible with the process according to the invention to prepare a VHP F VIII:C preparation whose specific volume-based activity is at least 200 IU/ml, with a specific activity of more than 2000 IU/mg. This concentration ensures that there are no problems with manipulation owing to the need to administer small volumes.

A preparation of this type does not need further stabilization by proteins, which avoids the risk of virus contamination. At the same time, the reduction in the high protein load means a considerable reduction in the stress on the immune system of the patient due to the addition of the albumin, which is unnecessary for the medicinal action, and of the unwanted impurities contained therein.

Since physiologically tolerated substances are added for the stabilization, no intolerance reactions occur on administration of the solution according to the invention.

EXAMPLE 1

Two VHP F VIII:C preparations were prepared, both by means of affinity chromatography on monoclonal anti-vWF Ig (method of Fulcher & Zimmermann PNAS (1982), 79, 1649) and dissociation of the vWF/F VIII:C complex by solution with a $CaCl_2$ concentration of 300 mM in 0.1 M acetate, 0.1 M lysine, pH 6.8 (eluate I), and by means of chromatography on monoclonal anti-F VIII:C Ig and elution of the F VIII:C by 50% ethylene glycol in 0.1 M acetate, 0.1 M lysine, pH 6.8 (eluate II). The specific F VIII:C activity determined in eluate I was 2500 IU/mg and 419 IU/ml, and in eluate II was 3280 IU/mg and 454 IU/ml. The two eluates were divided in each case. To one portion in each case was added in the ratio 1:1 by volume a 1% strength human albumin solution in 0.75% sucrose, 3% glycine and 0.1 mol/l NaCl (eluate I_{HSA}, eluate II_{HSA}). The stabilization buffer (0.75% sucrose, 3% glycine, 3% arginine, 0.05% ®Tween 80, pH 6.8) was likewise added 1:1 to the other half in each case (eluate I_S, eluate II_S). The albumin-containing samples were dialyzed against 0.75% sucrose, 3% glycine, 0.1 mol/l NaCl, pH 6.8, and the others against stabilization buffer. Dialysis was carried out at 4° C. for 16 hours with 1000-fold volume change. The F VIII:C activities were measured before and after the dialysis. Table 1 shows the F VIII:C activity in % relative to the total F VIII:C activity in the particular sample before dialysis.

TABLE 1

Eluate I_{HSA}	Eluate I_S	Eluate II_{HSA}	Eluate II_S
92	94	94	93

The results show that stabilization of the VHP F VIII:C eluates by means of the stabilization solution according to the invention is achieved irrespective of the preparation method and to the same extent as by addition of albumin.

EXAMPLE 2

An F VIII:C eluate with a specific F VIII:C activity of 3860 IU/mg of protein and 462 IU/ml was obtained after immunoaffinity chromatography on monoclonal anti-F VIII:C antibodies. Various stabilization solutions were added to this in the ratio 1:1 by volume, and it was dialyzed against the relevant stabilization solution as described in Example 1. A pH of 6.8 was adjusted in all solutions where appropriate with 10% acetic acid.

The following stabilization solutions were employed:

I. 0.75% sucrose, 0.4 M glycine, 0.15 M sodium chloride

II. 0.01M sodium citrate, 0.08 M glycine, 0.016 M lysine, 0.0025 M calcium chloride, 0.4 M sodium chloride

III. 1% sucrose, 0.14 M arginine, 0.1M sodium chloride

IV. 1% sucrose, 0.4 M glycine, 0.14 M arginine, 0.1M sodium chloride, 0.05% Tween 80

The F VIII:C activity was determined before and after the dialysis. In Table 2 the F VIII:C activity after dialysis is plotted in % relative to the relevant activity before dialysis.

TABLE 2

Mixture	I	II	III	IV
F VIII:C activity after dialysis for 16 hours	39.3%	35.1%	82.4%	96.2%

The solutions employed under I and II can be employed for the stabilization of albumin-free HP F VIII products with specific F VIII:C activities of 100–200 IU/mg, dispensing with addition of albumin. Solutions III and IV are suitable for stabilization of VHP F VIII preparations with specific F VIII:C activities greater than 1000 IU/mg.

I claim:

1. A stabilized solution with factor VIII:C activity containing factor VIII:C, an amino acid or one of its salts or homologs and a detergent or an organic polymer, wherein the specific factor VIII:C activity is at least 1000 IU/mg.

2. A solution as claimed in claim **1**, wherein the amino acid is a natural amino acid.

3. A solution as claimed in claim **1**, wherein the amino acid is a basic amino acid.

4. A solution as claimed in claim **1**, which contains arginine and glycine.

5. A solution as claimed in claim **1**, wherein the concentration of the amino acid is 0.001 to 1 mol/l.

6. A solution as claimed in claim **1**, which contains an organic polymer or a nonionic detergent.

7. A solution as claimed in claim **1**, wherein the F VIII:C activity is derived (a) from human factor VIII in its form which occurs in plasma or (b) from a genetically engineered factor VIII:C or (C) from a homolog of (a) or (b).

8. A pharmaceutical containing a solution as claimed in claim **1**.

9. A pharmaceutical as claimed in claim **8** further containing pharmaceutically compatible, stabilizing or buffering substances.

10. A pharmaceutical as claimed in claim **9**, which contains a carbohydrate.

11. A process for the preparation of a stable factor VIII:C solution which comprises adding an amino acid or one of its salts or homologs and an organic polymer or a detergent to a solution with factor VII I:C activity, wherein the specific factor VIII:C activity is at least 1000 IU/mg.

12. A stabilized solution as claimed in claim **1** containing an amino acid or one of its salts or homologs and an organic polymer, wherein the amino acid is arginine or glycine and the organic polymer is polyethylene glycol.

13. A stabilized solution as claimed in claim **1** containing an amino acid or one of its salts or homologs and a detergent, wherein the amino acid is arginine or glycine and the detergent is polyoxyethylene sorbitan mono-oleate.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,565,427
DATED : October 15, 1996
INVENTOR(S) : Dr. Wilfried FREUDENBERG

It is certified that error appears in the above-indentified patent and that said Letters Patent is hereby corrected as shown below:

Claim 7, column 4, line 41, "(C)" should read --(c)--.

Claim 9, column 4, line 44, after "claim 8", insert --,--.

Claim 11, column 4, line 52, "VII I:C" should read --VIII:C--.

Signed and Sealed this

Eighteenth Day of February, 1997

Attest:

BRUCE LEHMAN

Attesting Officer

Commissioner of Patents and Trademarks

EXHIBIT B

US005565427C1

(12) REEXAMINATION CERTIFICATE (4618th)

United States Patent
Freudenberg

(10) Number: US 5,565,427 C1
(45) Certificate Issued: Jul. 23, 2002

(54) **STABILIZED FACTOR VIII PREPARATIONS**

(75) Inventor: **Wilfried Freudenberg**, Cölbe-Schönstadt (DE)

(73) Assignee: **Aventis Behring GmbH**, Marburg (DE)

Reexamination Request:
No. 90/006,025, May 30, 2001

Reexamination Certificate for:

Patent No.:	5,565,427
Issued:	Oct. 15, 1996
Appl. No.:	08/235,241
Filed:	Apr. 29, 1994

Certificate of Correction issued Feb. 18, 1997.

Related U.S. Application Data

(63) Continuation of application No. 08/082,911, filed on Jun. 29, 1993, now abandoned, which is a continuation of application No. 07/864,610, filed on Apr. 7, 1992, now abandoned.

(30) **Foreign Application Priority Data**

Apr. 9, 1991 (DE) 41 11 393

(51) **Int. Cl.**[7] A61K 35/14; C07K 1/00; C07K 14/00

(52) **U.S. Cl.** 514/12; 514/21; 530/383

(58) **Field of Search** 514/12, 21; 530/383

(56) **References Cited**

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Primary Examiner—Jeffrey E. Russel

(57) **ABSTRACT**

The invention relates to stabilized solutions with F VIII coagulation activity, to a process for the preparation thereof and to the use thereof.

REEXAMINATION CERTIFICATE ISSUED UNDER 35 U.S.C. 307

NO AMENDMENTS HAVE BEEN MADE TO THE PATENT

AS A RESULT OF REEXAMINATION, IT HAS BEEN DETERMINED THAT:

The patentability of claims 1-13 is confirmed.

* * * * *

EXHIBIT C

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
90/006,823	10/21/2003	5565427	06478.0999-21000	6431

7590 10/11/2005

Finnegan Henderson Farabow Garrett & Dunner LLP
1300 I Street, NW
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EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Notice of Intent to Issue Ex Parte Reexamination Certificate	Control No.	Patent Under Reexamination
	90/006,823	5565427
	Examiner	Art Unit
	Holly Schnizer	1656

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

1. ☒ Prosecution on the merits is (or remains) closed in this ex *parte* reexamination proceeding. This proceeding is subject to reopening at the initiative of the Office or upon petition. *Cf.* 37 CFR 1.313(a). A Certificate will be issued in view of
   - (a) ☒ Patent owner's communication(s) filed: *08 August 2005*.
   - (b) ☐ Patent owner's late response filed: _____.
   - (c) ☐ Patent owner's failure to file an appropriate response to the Office action mailed: _____.
   - (d) ☐ Patent owner's failure to timely file an Appeal Brief (37 CFR 41.31).
   - (e) ☐ Other: _____.

   Status of *Ex Parte* Reexamination:
   - (f) Change in the Specification: ☐ Yes ☒ No
   - (g) Change in the Drawing(s): ☐ Yes ☒ No
   - (h) Status of the Claim(s):
     - (1) Patent claim(s) confirmed: *11*.
     - (2) Patent claim(s) amended (including dependent on amended claim(s)): *2-10,12 and 13*
     - (3) Patent claim(s) cancelled: *1*.
     - (4) Newly presented claim(s) patentable: 14-23.
     - (5) Newly presented cancelled claims: _____.

2. ☒ Note the attached statement of reasons for patentability and/or confirmation. Any comments considered necessary by patent owner regarding reasons for patentability and/or confirmation must be submitted promptly to avoid processing delays. Such submission(s) should be labeled: "Comments On Statement of Reasons for Patentability and/or Confirmation."

3. ☐ Note attached NOTICE OF REFERENCES CITED (PTO-892).

4. ☒ Note attached LIST OF REFERENCES CITED (PTO-1449 or PTO/SB/08).

5. ☐ The drawing correction request filed on _____ is: ☐ approved ☐ disapproved.

6. ☒ Acknowledgment is made of the priority claim under 35 U.S.C. § 119(a)-(d) or (f).
   a)☒ All b)☐ Some* c)☐ None of the certified copies have
   - ☐ been received.
   - ☐ not been received.
   - ☒ been filed in Application No. *07/864610*.
   - ☐ been filed in reexamination Control No. _____.
   - ☐ been received by the International Bureau in PCT Application No. _____.

   * Certified copies not received: _____.

7. ☒ Note attached Examiner's Amendment.

8. ☐ Note attached Interview Summary (PTO-474).

9. ☐ Other: _____.

cc: Requester (if third party requester)

UNITED STATES DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

REEXAMINATION

REASONS FOR PATENTABILITY / CONFIRMATION

Reexamination Control No. *90/006,823* Attachment to Paper No. *20050829*.

Art Unit *1656*.

The claims as amended, are now drawn to stabilized solutions of Factor VIII:C containing components not taught or suggested in the prior art of record. As stated in the communication mailed 7/14/04, there is no teaching or suggestion of adding a detergent or organic polymer with both glycine and arginine to a factor VIII:C solution in the prior art of record, therefore Claim 4 appears to be free of the prior art of record. Farb et al. and the prior art of record do not teach or suggest adding polyethylene glycol to a factor VIII solution having glycine or arginine and thus Claim 12 appears to be free of the prior art of record. Farb et al. teaches that the factor VIII solutions disclosed therein have specific activities ranging from 850-1800 IU/mg and potencies from 10-50 units/ml and thus does not meet the limitations of claims 14, 8, 9, 16-19, or 21-22 and a search of the prior art did not find any references teaching a factor VIII solution containing the same components of the claims wherein the factor VIII:C had a specific activity of greater than 2000 IU/mg. As stated in the Interview Summary of 2/23/05, the obviousness rejection of Claims 10 and 15 over Farb et al. in view of Coan et al. was withdrawn because there was no motivation to combine the references. Coan et al. teaches stabilizing proteins of high specific activity by adding carbohydrates. There would have been no motivation to combine the references because Coan et al. adds carbohydrates to proteins with higher specific activities than Farb et al. achieves and one of ordinary skill would not have had any expectation of success in stabilizing a protein with lower specific activity by adding carbohydrates. Claims 2, 3, 5-6, 7, 20, and 13 depend from Claim 15 and thus are free of the prior art for the same reasons as Claim 15. Claim 11 is free of the prior art of record because Farb et al. and the prior art do not teach adding an amino acid or its salts or homologs and an organic polymer or detergent to a factor VIII:C solution that already has specific activity of at least 1000 IU/mg prior to the addition of these components. The rejection of Claim 23 as unclear as to the amount of detergent added to the solution has been overcome by the addition of the units of V/V as indicated in the Advisory Action mailed 6/7/05. There is no teaching or suggestion of adding the specific concentrations of detergent to a stabilized factor VIII:C solution as claimed in claim 23. Thus, the amendments overcome all of the prior art rejections and appear to be patentable over the prior art of record.

The materials cited in the Information Disclosure Statement filed 5/25/05 with the Petition to Expunge under 37 CFR 1.59(b) have been considered and were not found to be important to a reasonable examiner in determining whether or not the claims are patentable.

(Examiner's Signature)

PTOL-476 (Rev. 03-98)

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER
Conferee

JON WEBER
SUPERVISORY PATENT EXAMINER
Conferee

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. The changes made by this examiner's amendment will be reflected in the reexamination certificate to issue in due course.

Authorization for this examiner's amendment was given in a telephone interview with Carol Einaudi on October 4, 2005.

The application has been amended as follows:

IN THE CLAIMS:

4. (Amended) A stabilized solution [as claimed in claim 1, which] with factor VIII:C activity containing factor VIII:C, an amino acid or one of its salts or homologs and a detergent or an organic polymer, wherein the specific factor VIII:C activity is at least 1000 IU/mg and wherein the stabilized solution contains arginine and glycine.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday through Thursday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Holly Schnizer
October 4, 2005